UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/787,067	02/25/2004	Scott S. Graves	295.061US4	3563

21186 7590 01/26/2007

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. BOX 2938
MINNEAPOLIS, MN 55402

EXAMINER	
BLANCHARD, DAVID J	
ART UNIT	PAPER NUMBER
1643	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

TH

Office Action Summary	Application No.	Applicant(s)	
	10/787,067	GRAVES ET AL.	
	Examiner	Art Unit	
	David J. Blanchard	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33,36-38,40-49 and 51* is/are pending in the application.

4a) Of the above claim(s) *11-26,48 and 49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10, 27-33, 36-38, 40-47 and 51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/31/05,4/4/05, 3/9/06, 8/7/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The preliminary amendments filed 31 July 2003 and 09 April 2004 have been entered in full.

2. Claims 1-33, 36-38, 40-49 and 51 are pending. It is noted that claim 52 is not pending in contrast to the reply filed 23 October 2006.

Election/Restrictions

3. Applicant's election of Group I, claims 1-10 and 27-49 in the reply filed on 23 October 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

4. Presently amended claims 48-49 are directed to an invention that is independent or distinct from the inventions originally claimed for the following reasons:

Inventions I and VI (presently amended claims 48-49) are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case the antibody of Group I can be used in a materially different method such as purifying the antigen in addition to the materially different therapeutic method of claims 48-49 (Group VI).

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 48-49 withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

5. Claims 11-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

6. Claims 34-35, 39, and 50 are cancelled.

Claim 51 has been added.

7. Claims 1-10, 27-33, 36-38, 40-47 and 51 are under consideration.

Oath/Declaration

8. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application-by-application number and filing date is required. See MPEP §§ 602.01 and 602.02.

> The oath or declaration is defective because it does not refer to the preliminary amendment present on the filing date of the instant application, which contains new matter (see item no. 9 below). During examination, if an examiner determines that a preliminary amendment that is present on the filing date of the application includes subject matter not otherwise supported by the originally filed specification and drawings, and the oath or declaration does not refer to the preliminary amendment, the examiner may require the applicant to file a supplemental oath or declaration under 37 CFR 1.67 referring to the preliminary amendment. In response to the requirement, applicant must submit (1) an oath or declaration that refers to the preliminary amendment, (2) an amendment that cancels the subject matter not supported by the originally filed specification and drawings, or (3) a request for reconsideration.

For applications filed prior to September 21, 2004, a preliminary amendment that was present on the filing date of an application may be considered a part of the original disclosure if it was referred to in a first filed oath or declaration in compliance with 37 CFR 1.63. If the preliminary amendment was not referred to in the oath or declaration, applicant will be required to submit a supplemental oath or declaration under 37 CFR 1.67 referring to both the application and the preliminary amendment filed with the original application. See MPEP 608.04(b).

Specification

9. The disclosure is objected to because of the following informalities:

a. The examiner acknowledges the preliminary amendment filed 2/25/2004 updating the benefit claim to prior applications at page 1 of the specification, however, the status of USSN 10/056,794 needs to be updated to indicate that USSN 10/056,794 is "now abandoned".

Appropriate correction is required.

b. The preliminary amendment filed 2/25/2004 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material, which is not supported by the original disclosure, is as follows: The amendment claims priority to Application No. 10/056,794, filed January 24, 2002, and now abandoned which is a continuation of Application No. 08/871,488, filed on June 9, 1997, which issued as U.S. Patent Application No. 6,358,710; which application is a continuation-in-part of U.S. Patent Application 08/660,362, filed on June 7, 1996 and now abandoned. The priority applications cannot be incorporated by reference after the original filing of the instant application. This objection can be overcome by removing the

incorporation by reference statement. Applicants' attention is directed to the "Oath/Declaration" section above.

See United States Patent and Trademark Office OG Notices: 1268 OG 89 (18 March 2003) "Benefit of Prior-Filed Application" (see Part VII).

Claim Rejections - 35 USC § 112

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

11. Claim 1-10, 27-33, 36-38, 40-47 and 51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 27-30 and 51 are indefinite in the recitation "antigen-binding antibody fragment of IgG class" in claims 27-28 as it is unclear what is contemplated by the phrase. Antibody classes are defined by heavy-chain antigenic determinants, called isotypic determinants, which distinguish constant region sites. Thus, while antigen-antibody fragments are produced from the various antibody classes (i.e., IgG, IgA, IgM, IgD and IgE), antigen-binding antibody fragments typically lack constant regions that could distinguish antibody classes, and one of skill in the art would not be reasonably apprised of what is contemplated by the phrase "antigen-binding antibody fragment of IgG class".

b. Claims 1-10, 30-33, 36-38 and 40-47 are vague and indefinite in the recitation of "NR-LU-13" and "NRX451" as the sole means of identifying the antibodies referred to

in the claims. The use of laboratory designations to identify a particular molecule renders the claims indefinite because different laboratories may use the same laboratory designations to define completely distinct molecules. This rejection can be overcome by amending the claims to specifically and uniquely identify antibodies "NR-LU-13" and "NRX451", for example, by SEQ ID number or by biological deposit number.

Claim Rejections - 35 USC § 112

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 1-10, 31-33, 36-38, 40-47 and 51 are rejected under 35 U.S.C. § 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention, because the specification does not provide evidence that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from the written description.

Claims 1-10, 31-33, 36-37 and 47 are drawn to antibody NR-LU-13 requiring a biological deposit to satisfy the statutory requirements for patentability under 35 U.S.C. 112. Applicants' receipt of deposit and Declaration of Deposit filed 2/25/2004 for cell line NR-LU-13 and assigned ATCC accession no. CRL-12360 that cell line NR-LU-13 was deposited in accordance with the Budapest treaty with the ATCC (10801 University Boulevard, Manassas, Virginia 20010-2209) on May 23, 1997, and that *all restrictions*

imposed on the availability to the public of the deposited cell line will be irrevocably removed upon the granting of a patent, is acknowledged, however, this is insufficient assurance that all of the conditions of 37 CFR 1.801-1.809 have been met in view of Applicant's earlier effective filing date, i.e., 6/7/1996. If a deposit is made after the effective filing date of the application for patent in the United States, as in the instant application, a verified statement is required from a person in a position to corroborate that the biological material described in the specification as filed is the same as that deposited in the depository, stating that the deposited material is identical to the biological material described in the specification and was in the applicant's possession at the time the application was filed. See MPEP 2406 and 37 CFR 1.804(b).

With respect to claims drawn to antibody NRX451, it is unclear if a cell line, which produces an antibody having the exact chemical identity of antibody NRX451 is known and publicly available, or can be reproducibly isolated without undue experimentation. Therefore, a suitable deposit for patent purposes is suggested. Without a publicly available deposit of the above cell line, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of: (1) the claimed cell line; (2) a cell line which produces the chemically and functionally distinct antibody claimed; and/or (3) the claimed antibody's amino acid or nucleic acid sequence is an unpredictable event.

For example, very different V_H chains (about 50% homologous) can combine with the same V_K chain to produce antibody-binding sites with nearly the same size, shape, antigen specificity, and affinity. A similar phenomenon can also occur when different V_H

sequences combine with different V_K sequences to produce antibodies with very similar properties. The results indicate that divergent variable region sequences, both in and out of the complementarity-determining regions, can be folded to form similar binding site contours, which result in similar immunochemical characteristics. Fundamental Immunology, William E. Paul, M.D. ed., 3rd ed. 1993, pg. 242. Therefore, it would require undue experimentation to reproduce the claimed antibody species antibody NRX451.

The specification lacks complete deposit information for the deposit of antibody NRX451. It is unclear whether antibodies possessing the identical properties of antibody NRX451 are known and publicly available or can be reproducibly isolated from nature without undue experimentation.

Exact replication of a cell line is an unpredictable event. Although applicant has provided a written description of a method for selecting the claimed hybridoma cell lines and monoclonal antibodies, this method will not necessarily reproduce hybridomas and antibodies which are chemically and structurally identical to those claimed. It is unclear that one of skill in the art could derive a hybridoma and monoclonal antibody identical to those claimed. Undue experimentation would be required to screen all of the possible hybridoma and antibody species to obtain the claimed antibodies.

Because one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed in the absence of the availability of the claimed antibody NRX451, a suitable deposit is required for patent purposes, evidence of public

availability of the claimed antibody or evidence of the reproducibility without undue experimentation of the claimed antibody, is required.

If the deposit is made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit of antibody NRX451 has been accepted by an International Depository Authority under the provisions of the Budapest Treaty and that all restrictions upon public access to the deposited material will be irrevocably removed upon the grant of a patent on this application. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State.

If the deposit of antibody NRX451 is not made under the provisions of the Budapest Treaty, then in order to certify that the deposit complies with the criteria set forth in 37 CFR 1.801-1.809 regarding availability and permanency of deposits, assurance of compliance is required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

> (a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request:
> (b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application:

(c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent of or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) the deposits will be replaced if they should become nonviable or non-replicable.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If a deposit is made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the biological material described in the specification as filed is the same as that deposited in the depository, stating that the deposited material is identical to the biological material described in the specification and was in the applicant's possession at the time the application was filed. See MPEP 2406 and 37 CFR 1.804(b).

Applicant's attention is directed to In re Lundak, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR 1.801-1.809 for further information concerning deposit practice.

Priority

14. Applicant claims priority to three previous applications in the preliminary amendment of 31 July 2003. Based on the information given by applicant and an

inspection of the priority applications, priority is not granted to USSN 08/660,362 for claims drawn to a humanized antibody or an antigen-binding fragment thereof wherein its N-linked glycosylation has been modified or chemically modified post expression to reduce its immunogenicity or toxicity and conjugates thereof (i.e., active agent and radionuclide) since this application does not disclose humanized antibodies modified post expression. Therefore, for purposes of applying prior art, the effective filing date of claims 1-3, 5-10, 27-33, 36-38, 40-45, 47 and 51 as they pertain to humanized antibodies modified post expression is deemed to be that of USSN 08/871,488, i.e., 6/9/1997.

Should the applicant disagree with the examiner's factual determination above, it is incumbent upon the applicant to provide the specific page number(s) of USSN 08/660,362, which specifically supports the particular claim limitation for each and every claim limitation in all the pending claims which applicant considers to have been in possession of and fully enabled for prior to the effective filing date of 6/9/1997.

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 27, 29 and 51 are rejected under 35 U.S.C. 102(b) as being anticipated by Weitzhandler et al (Journal of Pharmaceutical Sciences, 83(12):1670-1675, December 1994, Ids reference filed 8/7/2006).

The claims are being interpreted as drawn to an antibody or antigen-binding

fragment thereof of the IgG class wherein its N-linked glycosylation has been chemically modified post expression.

Weitzhandler et al teach a humanized monoclonal antibody (humanized MAb M115) that is de-N-glycosylated by treatment with PNGase F, wherein the humanized antibody is interpreted to be a "therapeutic antibody" (see entire document, particularly pg. 1672 1st column, Fig. 2 parts B and C and Table 3). Thus, the treatment of humanized MAb M115 with PNGase F occurs "post expression", i.e., after the production of the polypeptide.

Thus, Weitzhandler et al anticipate the claims.

Claim Rejections - 35 USC § 103

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

18. Claims 1-4, 10, 31-33 and 36-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morgan et al (US Patent 5,084,396, issued 1/28/1992, Ids reference filed 1/31/2005) as evidenced by Graves et al (Clinical Cancer Research, 5:899-908, April 1999) in view of Queen et al (US Patent 5,530,101, filed 12/19/1990, Ids reference filed 1/31/2005) and Co et al (US Patent 5,714,350, 3/9/1992, Ids reference filed 8/7/2006) and Duncan et al (Nature, 332:738-740, 1988, IDS filed 1/31/2005).

The claims are being interpreted as drawn to a humanized antibody or antigen-binding fragment thereof that specifically binds to the antigen bound by antibody NR-LU-13 and wherein said humanized antibody or antigen-binding fragment thereof does not possess N-linked glycosylation and does not possess O-linked glycosylation wherein said humanized antibody or antigen-binding fragment thereof has been mutated to prevent N-linked glycosylation and wherein the humanized antibody or antigen-binding fragment thereof is conjugated to a ligand or anti-ligand, which is biotin, avidin or streptavidin, or is conjugated to a diagnostic or therapeutic agent and wherein

the humanized antibody or antigen-binding fragment thereof has been expressed in insect cells, mammalian cells, bacterial cells or yeast.

Morgan et al teach monoclonal antibodies that bind the NR-LU-10 antigen expressed in carcinomas (see entire document, particularly Ex. 6 at col. 18-19). As evidenced by Graves et al, NR-LU-13 is a chimeric version of the murine NR-LU-10 antibody and as such contains the same Fv and the same antigen specificity (see entire document, particularly pg. 900, 1st col, 1st par.). Morgan et al do not specifically teach aglycosylated tumor specific humanized antibodies or antigen-binding fragments thereof conjugated to biotin, avidin, streptavidin, a diagnostic or therapeutic agent for therapeutic benefit in human cancer patients, wherein N- and O-linked glycosylation site sequences have been substituted or deleted by site-directed mutagenesis (i.e., mutated to prevent N-linked glycosylation). These deficiencies are made up for in the teachings of Queen et al and Co et al and Duncan et al.

Queen et al teach humanized antibodies and antigen-binding fragments thereof that are less immunogenic in human patients compared to mouse and chimeric antibodies and conjugates thereof comprising conjugation of the antibodies to a diagnostic or therapeutic agent for cancer therapy including the use of biotin-avidin and wherein the humanized antibodies are expressed in bacteria, yeast or mammalian host cells (see entire document, particularly col, 1, 12-16, 19-20 and 40, Fig.8A-8B description).

Co et al teach a humanized antibody and antigen-binding fragments thereof including F(ab')2, Fv and Fab wherein site-directed mutagenesis (i.e., substitution or

deletion) is used to destroy N- and O-linked glycosylation site sequences in the humanized antibody and antigen-binding fragments thereof that may be expressed in bacteria, yeast and mammalian cells, wherein the aglycosylated humanized antibody and antigen-binding fragments thereof have increased affinity and are useful for cancer diagnosis and therapy (see entire document, particularly col. 2, 4, 6-8, 9 and 11, lines 17-23).

Duncan et al teach a method of removing the N-linked glycosylation site at Asn-297 in the CH2 domain of the constant region of IgG by site-directed mutagenesis wherein the Asn 297→Ala mutation eliminates the ability of IgG to fix complement and reduced the antibody affinity for C1q about threefold (see page 738 right column and Fig. 1).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced tumor specific aglycosylated humanized antibodies that bind to the same antigen bound by antibody NR-LU-10 conjugated to a diagnostic or therapeutic agent or biotin for therapeutic benefit in human cancer patients, wherein N- and O-linked glycosylation site sequences have been substituted or deleted by site-directed mutagenesis.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have produced tumor specific aglycosylated humanized antibodies that bind to the same antigen bound by antibody NR-LU-10 conjugated to a diagnostic or therapeutic agent or biotin for therapeutic benefit in human cancer patients, wherein N- and O-linked

glycosylation site sequences have been substituted or deleted by site-directed mutagenesis in view of Morgan et al as evidenced by Graves et al in view of Queen et al and Co et al and Duncan et al because Morgan et al teach monoclonal antibodies that bind the NR-LU-10 antigen expressed in carcinomas, which is the same antigen bound by antibody NR-LU-13 as evidenced by Graves and Queen et al teach humanized antibodies and antigen-binding fragments thereof that are less immunogenic in human patients compared to mouse and chimeric antibodies and conjugates thereof comprising conjugation of the antibodies to a diagnostic or therapeutic agent for cancer therapy including the use of biotin-avidin and Co et al teach site-directed mutagenesis and expression in bacteria, yeast and mammalian hosts to destroy N- and O-linked glycosylation site sequences in humanized antibodies and antigen-binding fragments thereof for cancer diagnosis and therapy and elimination of N- and O-linked glycosylation site sequences increases antibody affinity and Duncan et al teach a method of removing the N-linked glycosylation site at Asn-297 in the CH2 domain of the constant region of IgG by site-directed mutagenesis wherein the Asn 297→Ala mutation eliminates the ability of IgG to fix complement and reduced the antibody affinity for C1q about threefold, which suggests the possibility of obtaining antibodies devoid of select biological functions. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to modify the humanized antibodies of Morgan et al according to the teachings of Queen et al and Co et al and Duncan et al to produce aglycosylated humanized antibodies and antigen-binding fragments thereof that are less immunogenic in human cancer patients and have increased affinity for antigen and offer

the additional advantages of reducing or tailoring antibody effector functions, for immunodiagnosis and immunotherapy in human cancer patients. The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. *In re Semaker*, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983). Further, one of ordinary skill in the art would have had a reasonable expectation of success in making the above modifications in view of the teachings of Co et al and Duncan et al, providing evidence that carbohydrate depletion does not reduce antigen specificity or affinity of the antibodies. Thus, it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to have produced tumor specific aglycosylated humanized antibodies that bind to the same antigen bound by antibody NR-LU-10 conjugated to a diagnostic or therapeutic agent or biotin for therapeutic benefit in human cancer patients, wherein N- and O-linked glycosylation site sequences have been substituted or deleted by site-directed mutagenesis in view of Morgan et al as evidenced by Graves et al in view of Queen et al and Co et al and Duncan et al.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

19. Claims 1-3, 5-9, 27-33, 36-37 and 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morgan et al (US Patent 5,084,396, issued 1/28/1992, Ids

reference filed 1/31/2005) as evidenced by Graves et al (Clinical Cancer Research, 5:899-908, April 1999) in view of Queen et al (US Patent 5,530,101, filed 12/19/1990, Ids reference filed 1/31/2005) and Awwad et al [a] (US Patent 5,856,106, 11/1/1995, Ids reference filed 8/7/2006) and Awwad et al [b] (Cancer Immunology and Immunotherapy, 38(1):23-30, January 1994).

The claims are being interpreted as drawn to a humanized antibody or antigen-binding fragment thereof that specifically binds to the antigen bound by antibody NR-LU-13 wherein its N-linked glycosylation has been chemically modified post expression by oxidation followed by stabilization of the aldehydes generated by oxidation or followed by reduction to reduce immunogenicity or toxicity and wherein the humanized antibody or antigen-binding fragment thereof is conjugated to a ligand or anti-ligand, which is biotin, avidin or streptavidin, or is conjugated to a diagnostic or therapeutic agent.

Morgan et al have been described supra. Morgan et al do not specifically teach aglycosylated tumor specific humanized antibodies or antigen-binding fragments thereof conjugated to biotin, avidin, streptavidin, a diagnostic or therapeutic agent, wherein N- and O-linked glycosylation site sequences have been substituted or deleted by site-directed mutagenesis (i.e., mutated to prevent N-linked glycosylation). These deficiencies are made up for in the teachings of Queen et al and Awwad et al [a] and Awwad et al [b].

Queen et al have been described supra.

Awwad et al [a] teach that chemical modification of monoclonal antibody carbohydrates by oxidation, enzymatically or by the use of glycosylation inhibitors reduces the immunogenicity of the antibodies when administered in a patient and the antibodies are conjugated to a diagnostic agent including the use of avidin and biotin (see entire document, particularly, col. 1, lines 51-63, col. 4-5, col. 10, line 49 to col. 11 and Table 6).

Awwad et al [b] teach modification of anti-tumor monoclonal antibody carbohydrates by oxidation and subsequent conjugation in which some of the aldehydes become coupled to a peptide linker/chelator (GYK-DTPA) or a cytotoxic drug (doxorubicin adipic dihydrazide; ADR-ADH) and some are reduced to alcohols during subsequent reduction (i.e., the aldehydes are stabilized following oxidation) (see entire document, particularly pp. 24, 27-29).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced tumor specific aglycosylated humanized antibodies that bind to the same antigen bound by antibody NR-LU-10 conjugated to a diagnostic or therapeutic agent or biotin for therapeutic benefit in human cancer patients wherein N-linked glycosylation has been modified post expression by oxidation followed reduction.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have produced tumor specific aglycosylated humanized antibodies that bind to the same antigen bound by antibody NR-LU-10 conjugated to a diagnostic or therapeutic agent or

biotin for therapeutic benefit in human cancer patients wherein N-linked glycosylation has been modified post expression by oxidation followed reduction in view of Morgan et al as evidenced by Graves et al and in view of Awwad et al [a] and Awwad et al [b] because Morgan, Jr. et al teach monoclonal antibodies that bind the NR-LU-10 antigen expressed in carcinomas, which is the same antigen bound by antibody NR-LU-13 as evidenced by Graves and Queen et al teach humanized antibodies and antigen-binding fragments thereof that are less immunogenic in human patients compared to mouse and chimeric antibodies and conjugates thereof comprising conjugation of the antibodies to a diagnostic or therapeutic agent for cancer therapy including the use of biotin-avidin and Awwad et al [a] teach chemical modification of monoclonal antibody carbohydrates by oxidation, enzymatically, or by the use of glycosylation inhibitors reduces the immunogenicity of the antibodies when administered in a patient and the antibodies are conjugated to a diagnostic agent including the use of avidin and biotin and Awwad et al [b] teach modification of anti-tumor monoclonal antibody carbohydrates by oxidation and subsequent conjugation in which some of the aldehydes become coupled to a peptide linker/chelator (GYK-DTPA) or a cytotoxic drug (doxorubicin adipic dihydrazide; ADR-ADH) and some are reduced to alcohols during subsequent reduction. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated by the goal of reducing the immunogenicity of the antibodies of Morgan et al according to the teachings of Queen and produce humanized antibodies and antigen-binding fragments thereof that bind the same tumor antigen as antibody NR-LU-10 (i.e., the antigen bound by NR-LU-13; chimeric version of

antibody NR-LU-10) and further reduce the immunogenicity of the humanized antibodies by chemical oxidation followed by conjugation to a cytotoxic moiety and subsequent reduction as taught by Awwad et al [a] and [b] for therapeutic benefit in human cancer patients. Thus, there would be an advantage to producing aglycosylated tumor specific humanized antibodies conjugated to a radionuclide, chemotherapeutic agent or toxin for therapeutic benefit in human cancer patients. Thus, it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to have produced tumor specific aglycosylated humanized antibodies that bind to the same antigen bound by antibody NR-LU-10 conjugated to a diagnostic or therapeutic agent or biotin for therapeutic benefit in human cancer patients wherein N-linked glycosylation has been modified post expression by oxidation followed reduction in view of Morgan et al as evidenced by Graves et al and in view of Queen et al and Awwad et al [a] and Awwad et al [b].

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

20. Claims 31-33, 36-37 and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morgan et al (US Patent 5,084,396, issued 1/28/1992, Ids reference filed 1/31/2005) as evidenced by Graves et al (Clinical Cancer Research, 5:899-908, April 1999) in view of Queen et al (US Patent 5,530,101, filed 12/19/1990, Ids reference filed 1/31/2005).

The claims are being interpreted as drawn to a humanized antibody or antigen-binding fragment thereof that specifically binds to the antigen bound by antibody NR-LU-13 wherein the humanized antibody or antigen-binding fragment thereof is conjugated to a ligand or anti-ligand, which is biotin, avidin or streptavidin, or is conjugated to a diagnostic or therapeutic agent and a pharmaceutical composition comprising the conjugated humanized antibody and a pharmaceutically acceptable carrier or diluent and wherein the humanized antibody or antigen-binding fragment thereof has been expressed in insect cells, mammalian cells, bacterial cells or yeast.

Morgan et al as evidenced by Graves et al have been described supra. Morgan et al do not specifically teach wherein the humanized antibody or antigen-binding fragment thereof that specifically binds to the antigen bound by antibody NR-LU-13 wherein the humanized antibody or antigen-binding fragment thereof is conjugated to a ligand or anti-ligand, which is biotin, avidin or streptavidin, or is conjugated to a diagnostic or therapeutic agent and wherein the humanized antibody or antigen-binding fragment thereof has been expressed in insect cells, mammalian cells, bacterial cells or yeast. These deficiencies are made up for in the teachings of Queen et al.

Queen et al have been described supra. Queen et al also teach pharmaceutical compositions comprising a humanized antibody or antigen-binding fragment thereof conjugated to a diagnostic or therapeutic agent and a pharmaceutically acceptable carrier, which were "known or apparent to those skilled in the art" (see col. 23 and col. 19-20).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced a humanized antibody or antigen-binding fragment thereof that binds to the same carcinoma antigen bound by antibody NR-LU-10, wherein the humanized antibody or antigen-binding fragment thereof is expressed in bacteria, yeast and mammalian host cells and is conjugated to a diagnostic or therapeutic agent or biotin and is present in a pharmaceutical composition comprising a pharmaceutically acceptable carrier for therapeutic benefit in human cancer patients.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time the invention was made to have produced a humanized antibody or antigen-binding fragment thereof that binds to the same carcinoma antigen bound by antibody NR-LU-10, wherein the humanized antibody or antigen-binding fragment thereof is expressed in bacteria, yeast and mammalian host cells and is conjugated to a diagnostic or therapeutic agent or biotin and is present in a pharmaceutical composition comprising a pharmaceutically acceptable carrier for therapeutic benefit in human cancer patients in view of Morgan et al as evidenced by Graves et al in view of Queen et al because Morgan et al teach monoclonal antibodies that bind the NR-LU-10 antigen expressed in carcinomas, which is the same antigen bound by antibody NR-LU-13 as evidenced by Graves and Queen et al teach humanized antibodies and antigen-binding fragments thereof that are less immunogenic in human patients compared to mouse and chimeric antibodies and conjugates thereof comprising conjugation of the antibodies to a diagnostic or

therapeutic agent for cancer therapy including the use of biotin-avidin for detection as well as the use of suitable host cells for the expression of the humanized antibodies such as bacteria, yeast and mammalian host cells and pharmaceutical compositions comprising the humanized antibody conjugate and a pharmaceutically acceptable carrier. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated by the goal of reducing the immunogenicity of the antibodies that bind the same carcinoma antigen bound by NR-LU-10 as taught by Morgan et al according to the teachings of Queen et al and produce humanized antibodies and antigen-binding fragments thereof that bind the same carcinoma antigen bound by NR-LU-10 and are less immunogenic in human cancer patients and are conjugated to a therapeutic or diagnostic agent including using biotin-avidin for detection and therapy in human cancer patients. Thus, there would have been an advantage to rendering the antibodies of Morgan et al less immunogenic in human cancer patients and better suited for the delivery of a diagnostic or therapeutic agent to tumor sites in human cancer patients. Thus, it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to have produced a humanized antibody or antigen-binding fragment thereof that binds to the same carcinoma antigen bound by antibody NR-LU-10, wherein the humanized antibody or antigen-binding fragment thereof is expressed in bacteria, yeast and mammalian host cells and is conjugated to a diagnostic or therapeutic agent or biotin and is present in a pharmaceutical composition comprising a pharmaceutically acceptable carrier for

therapeutic benefit in human cancer patients in view of Morgan et al as evidenced by Graves et al in view of Queen et al.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Double Patenting

21. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

22. Claims 1-10, 27-30, 41-46 and 51 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 6,358,710 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are drawn to a humanized antibody or antigen-binding fragment thereof that specifically binds to the

antigen bound by antibody NR-LU-13 or is the humanized antibody NRX451 and wherein the humanized antibody or antigen-binding fragment thereof does not possess N-linked glycosylation and O-linked glycosylation has been reduced or eliminated wherein said humanized antibody or antigen-binding fragment thereof has been mutated to prevent N-linked glycosylation or wherein the glycosylation has been modified post expression by oxidation followed by stabilization of the aldehydes or followed by reduction and claims 1-6 of U.S. Patent No. 6,358,710 B1 are drawn to humanized antibody NRX 451 or an antigen-binding fragment thereof that either does not possess N-linked glycosylation to reduce immunogenicity or toxicity and wherein the humanized antibody (NRX 451) binds to the antigen bound by NR-LU-13 wherein the polynucleotides encoding said humanized antibody or said antigen-binding fragment thereof have been substituted or deleted in the glycosylation motif Asn-Xaa-Ser(Thr) of the CH2 domain to prevent N-linked glycosylation in the CH2 domain wherein Xaa is any amino acid and Ser and Thr are interchangeable or the glycosylation has been chemically modified post expression to reduce immunogenicity or toxicity, wherein the chemical modification is oxidation followed by stabilization of the aldehydes generated by oxidation or followed by reduction. Thus, claims 1-6 of U.S. Patent No. 6,358,710 B1 are drawn to a species that reads on the genus claims as well as the species claims (i.e., also drawn to humanized antibody NRX 451) of the present application.

Claims 31-33, 36-38, 40 and 47 are obvious variants of claim 1 of U.S. Patent No. 6,358,710 B1 in view of the prior art.

23. Claims 31-33, 36-38, 40 and 47 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,358,710 B1 in view of Queen et al (US Patent No. 5,530,101, filed 12/19/1990, Ids reference filed 1/31/2005).

Claims 31-33, 36-38, 40 and 47 are drawn to a humanized antibody or antigen-binding fragment thereof that specifically binds to the antigen bound by antibody NR-LU-13 or is humanized antibody NRX 451 wherein the humanized antibody or antigen-binding fragment thereof is conjugated to a ligand or anti-ligand, which is biotin, avidin or streptavidin, or is conjugated to a diagnostic or therapeutic agent and a pharmaceutical composition comprising the conjugated humanized antibody and a pharmaceutically acceptable carrier or diluent and wherein the humanized antibody or antigen-binding fragment thereof has been expressed in insect cells, mammalian cells, bacterial cells or yeast.

Claim 1 of U.S. Patent No. 6,358,710 B1 has been described supra. Claim 1 of U.S. Patent No. 6,358,710 B1 does not recite wherein humanized NRX 451 or an antigen-binding fragment thereof is conjugated to a ligand or anti-ligand, which is biotin, avidin or streptavidin, or is conjugated to a diagnostic or therapeutic agent and a pharmaceutical composition comprising the conjugated humanized antibody and a pharmaceutically acceptable carrier or diluent and wherein the humanized antibody or antigen-binding fragment thereof has been expressed in insect cells, mammalian cells, bacterial cells or yeast. These deficiencies are made up for in the teachings of Queen et al.

Queen et al have been described supra.

Claims 31-33, 36-38, 40 and 47 in the present application are obvious variants of claim 1 of U.S. Patent 6,358,710 B1 because it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to produce humanized antibody NRX 451 by expression in bacteria, yeast or mammalian cells and conjugate the humanized antibody or antigen binding fragment thereof to a diagnostic or therapeutic agent and produce a pharmaceutical composition comprising the conjugated NRX 451 humanized antibody or antigen binding fragment thereof and a pharmaceutically acceptable carrier or diluent for therapeutic benefit in human cancer patients.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success at the time then invention was made to produce humanized antibody NRX 451 by expression in bacteria, yeast or mammalian cells and conjugate the humanized antibody or antigen binding fragment thereof to a diagnostic or therapeutic agent and produce a pharmaceutical composition comprising the conjugated NRX 451 humanized antibody or antigen binding fragment thereof and a pharmaceutically acceptable carrier or diluent for therapeutic benefit in human cancer patients in view of claim 1 of U.S. Patent 6,358,710 B1 and Queen et al because Queen et al teach that humanized antibodies and antigen-binding fragments thereof are less immunogenic in human patients compared to mouse and chimeric antibodies and conjugating the humanized antibodies to a diagnostic or therapeutic agent for cancer therapy including the use of biotin-avidin for detection as well as the use of suitable host

cells such as bacteria, yeast and mammalian cells for the expression of humanized antibodies and pharmaceutical compositions comprising the humanized antibody conjugate and a pharmaceutically acceptable carrier to facilitate the administration in human cancer patients and which were "known or apparent to those skilled in the art" (see col. 23). Therefore, one of ordinary skill in the art would have been motivated to produce the humanized antibody NRX 451 or an antigen binding fragment thereof by expression in suitable host cells (i.e., bacteria, yeast and mammalian cells) and conjugate humanized antibody NRX 451 to a diagnostic or therapeutic agent for the advantages immunodetection and immunotherapy in human cancer patients or preferably provide the conjugated humanized antibody NRX 451 as a pharmaceutical composition comprising a pharmaceutically acceptable carrier to facilitate administration in human cancer patients. Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce humanized antibody NRX 451 by expression in bacteria, yeast or mammalian cells and conjugate the humanized antibody or antigen binding fragment thereof to a diagnostic or therapeutic agent and produce a pharmaceutical composition comprising the conjugated NRX 451 humanized antibody or antigen binding fragment thereof and a pharmaceutically acceptable carrier or diluent for therapeutic benefit in human cancer patients in view of claim 1 of U.S. Patent 6,358,710 B1 and Queen et al.

24. Claims 1-10, 27-30, 32, 36, 47 and 51 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 74-

77 and 85-87 of copending Application No. 10/787,067 in view of Morgan et al (US Patent 5,084,396, issued 1/28/1992, Ids reference filed 1/31/2005) as evidenced by Graves et al (Clinical Cancer Research, 5:899-908, April 1999) in view of Queen et al (US Patent 5,530,101, filed 12/19/1990, Ids reference filed 1/31/2005). Although the conflicting claims are not identical, they are not patentably distinct from each other.

Instant claims 1-10, 27-30, 32, 36, 47 and 51 have been described supra.

Claims 74-77 and 85-87 of copending Application No. 10/631,660 are drawn to a humanized antibody or antigen-binding fragment thereof that does not possess N-linked glycosylation or its N-linked glycosylation has been modified or chemically modified post expression to reduce immunogenicity or toxicity and said humanized antibody or antigen-binding fragment thereof that also does not possess O-linked glycosylation and wherein the polynucleotides encoding said humanized antibody or antigen-binding fragment thereof have been substituted or deleted to prevent N-linked glycosylation and wherein the humanized antibody or antigen-binding fragment thereof is conjugated to a radionuclide, a drug, an anti-tumor agent or toxin (i.e., interpretation of an "active agent") or conjugated to an imaging agent that is a radionuclide selected from ^{99m}Tc, ^{111}In and ^{18}F. Claims 74-77 and 85-87 of copending Application No. 10/631,660 do not specifically teach a humanized antibody or antigen binding fragment thereof that binds the same antigen bound by NR-LU-13 wherein the conjugated humanized antibody or antigen-binding fragment thereof is formulated as a pharmaceutical composition comprising a pharmaceutically acceptable carrier or the expression of the humanized

antibody in bacteria, yeast or mammalian host cells. These deficiencies are made up for in the teachings of Morgan et al and Queen et al.

Morgan et al have been described supra.

Queen et al have been described supra.

Claims 1-10, 27-30, 32, 36, 47 and 51 of the present application are obvious variants of claims 74-77 and 85-87 of copending Application No. 10/631,660 because it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced a humanized antibody or antigen-binding fragment thereof that binds to the same antigen as bound by antibody NR-LU-10 according to claims 74-77 and 85-87 of copending Application No. 10/631,660 wherein the humanized antibody is expressed in bacteria, yeast or mammalian host cells and is provided as a pharmaceutical composition comprising the humanized antibody and a pharmaceutically acceptable carrier for therapeutic benefit in human carcinoma patients.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to at the time the invention was made to have produced an aglycosylated humanized antibody or antigen-binding fragment thereof that binds to the same antigen as bound by antibody NR-LU-10 according to claims 74-77 and 85-87 of copending Application No. 10/631,660 wherein the humanized antibody is expressed in bacteria, yeast or mammalian host cells and is provided as a pharmaceutical composition comprising the humanized antibody and a pharmaceutically acceptable carrier for therapeutic benefit in human carcinoma patients in view of

Morgan et al and Queen et al because Morgan et al teach monoclonal antibodies that bind the NR-LU-10 antigen expressed in carcinomas, which is the same antigen bound by antibody NR-LU-13 as evidenced by Graves and Queen et al teach humanized antibodies and antigen-binding fragments thereof that are less immunogenic in human patients compared to mouse and chimeric antibodies and suitable host cells for the expression of the humanized antibodies such as bacteria, yeast and mammalian host cells and pharmaceutical compositions comprising a humanized antibody conjugated to a diagnostic agent and a pharmaceutically acceptable carrier. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to produce an aglycosylated humanized antibody or antigen-binding fragment thereof that bind the same antigen bound by antibody NR-LU-10, which is expressed in carcinomas and one of ordinary skill in the art would have been motivated to produce the humanized antibody using any known suitable host cell as taught by Queen (i.e., bacteria, yeast, or mammalian host cells) and produce a pharmaceutical composition comprising the radiolabeled humanized antibody and a pharmaceutically acceptable carrier to facilitate administration for imaging carcinoma cells in human patients. Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have produced an aglycosylated humanized antibody or antigen-binding fragment thereof that binds to the same antigen as bound by antibody NR-LU-10 according to claims 74-77 and 85-87 of copending Application No. 10/631,660 wherein the humanized antibody is expressed in bacteria, yeast or mammalian host cells and is provided as a pharmaceutical composition comprising the humanized

antibody and a pharmaceutically acceptable carrier for therapeutic benefit in human carcinoma patients in view of Morgan et al and Queen et al.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim 1-10, 27-30, 32, 36, 47 and 51 are directed to an invention not patentably distinct from claims 74-77 and 85-87 of commonly assigned copending Application No. 10/631,660 in view of Goldenberg. Specifically, see above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned copending Application No. 10/631,660, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

Conclusion

25. No claim is allowed.

26. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Bieniarz et al. U.S. Patent 5,191,066.

Shih et al. U.S. Patent 5,057,313.

Rodwell et al. U.S. Patent 5,047,227.

Ultee et al. U.S. Patent 4,937,183.

27. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832.

The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
David J. Blanchard
571-272-0827